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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/569,866	02/28/2006	Borek Zaludek	J187-030 US	9742

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Peter C Michalos
Notaro & Michalos
Suite 110
100 Dutch Hill Road
Orangeburg, NY 10962-2100

EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/569,866	ZALUDEK ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/22/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed **1/22/08** presents remarks and arguments to the office action mailed **11/6/07**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of Claims

Claims 1-5 are pending in this office action. Claim 4 is amended.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant amended the claim and the rejection is withdrawn.

Response to argument under 103 rejection

Applicant argues that: The application is looking for solution according to the present application ran into difficulties when replacing lactose with an alcoholic sugar of non-animal origin, to eliminate a risk of viral contamination in a pharmaceutical composition.

Secondly, that Bouloumie teaches a composition of oxaliplatin, mannitol and alanine, that the freeze drying is not evidently accompanied.
Also, that the freeze-dried composition of Dexter comprises a weight ratio of 1:4.5, that the instant claim 4 is not obvious .

In response, taking the first argument, there is no where in the claims that talks or recite the difficulty in (such as viral contamination) preparing the claimed composition. One skill in the art would have been motivated to take into consideration several factors such as contamination, stability, and toxicity when preparing a pharmaceutical compositon as these are given to patients. These considerations are silently factored in pharmaceutical preparation. See entire document of Guide to inspects of Bulk Pharmaceutical Chemicals.

Next, that Bouloumie teaches a composition of oxaliplatin, mannitol and alanine, that the freeze drying is not evidently accompanied. This is found not persuasive. Boulomie et al. teach a freeze-dried pharmaceutical formulation, wherein the active agent is oxaliplatin. There are several ways/methods of freeze drying, it is within the purview of one of ordinary skill in the art as to what type to use. Clearly the reference teaches a freeze dried pharmaceutical with the same compound. Specifically a vacuo

freezing which Applicant is claiming. Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic.

Also as stated in the MPEP, "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. In re Fitzgerald, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

Lastly, the freeze dried composition of Dexter comprises a weight ratio of 1:4.5, that the instant claim 4 is not obvious. The range is 1:3 to 1:7, is 1:4.5 not within the claim range? How is that not obvious? As to one of ordinary skill would not have found claim 4 obvious is not persuasive for the same reason given above.

The rejection is maintained.

Maintained Claim Rejections - 35 USC § 103

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bouloumie et al., US 6,284,277 in view of Dexter et al., US 6,063,780.

Boulomie et al. teach a freeze-dried pharmaceutical formulation, wherein the active agent is oxaliplatin. See col6, lines 58-60 and col. 7, line 7. The reference also teaches the active agent is freeze-dried in a formulation of mannitol (an alcoholic sugar). See col. 10, lines 10-30 as required by instant claims 1-3 and 4(in part). As to instant claim 5, oxaliplatin is a known anticancer agent belongs to the group of platinum drug derivatives, therefore one of ordinary skill in the art would have been motivated to use oxaliplatin for the treatment of cancer.

The above reference, however, fail to teach the range of oxaliplatin and the non-alcoholic sugar.

Dexter et al. teach administering an effective amount of a platinum complex compound (see abstract) in a freeze-dried formulation in a concentration of 1:4.5 of the alcoholic sugar lactose. See col. 5, lines 60-63. (For example, 100 mg of oxaliplatin is used with 450 mg of lactose, then the ratio is 1:4.5), which is within the claim limitation of claims 1 and 4. The formulation is used for the treatment of tumors, see col. 6, lines 13+.

One of ordinary skill in the art would have been motivate to substitute the alcoholic sugar lactose with that of mannitol and freeze –dry the formulation in a concentration recited by Dexter et al. for the administration to tumor patients as taught by Dexter et al. See col. 6, lines 13+.

As to the procedure on how to freeze-dry the formulation, one of ordinary skill in the art would follow the manual procedure for freeze-drying based on the instrument used. It is common knowledge to refrigerate or place on ice the composition for freeze-drying before attempting freeze-drying. As evidence by Laboratory procedures for microorganisms, the vials containing the active agent is place at –20 ° C before the freeze drying procedure. Bouloumie et al. teach the rate of freezing in a vacuo is -2° C/min. University of Cambridge discloses that there are lots of different ways of lyophilizing or removing water, and the process chosen to formulate a particular drug will depend on the intended delivery method as well as the stability of the substance as evidence by.

New Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ibrahim et al. WO 94/12193 taken with Bouloumie et al., US 6,284,277 in view of Dexter et al., US 6,063,780.

Ibrahim et al, teach a freeze –dried composition comprising oxaliplatin and a mannitol, see abstract and page 7 example 2. the reference also teaches the composition is placed (60 ml) in a vial (falcon). It is understood that the size of the container is not taught, however, 60 ml is equated to occupying 60% of the capacity of the vial, cooled and freeze dried at temperatures of -50. See pages 9, lines 9-16. The reference teaches the composition is used to treat cancers , see page 1, lines 13-15.

Boulomie and Dexter are applied here as above and the reasons are also applied here.

One of ordinary skill in the art would have been motivated to combine the cited prior art of Ibrahim et al. with boulomie and Dexter because freeze dried oxaliplatin have

been taught in the prior art of record. The cited references disclose a freeze-dried composition having a mannitol (alcoholic sugar) with oxaliplatin in a ration of 1:4,5.

It would have been obvious to have made a freeze-dried composition that comprises oxaliplatin and mannitol because it is known in the art. As with the concentration it is within the purview of the artisan to optimize. And as stated above, freeze drying is obvious to one of ordinary skill in the art, nothing unobvious is seen in the art of freeze. Every single lyopholyzer comes with a manual that tells the temperature ranges and under what parameters are best for a variety of products and combination. This is known in the art.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
4/17/08

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614